REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 20-37 were pending in this application when last examined. Claims 27-32 and 35-37 were withdrawn as non-elected subject matter. Claims 20-26, 33 and 34 were examined and stand rejected.

Claims 20, 23, 24, and 25 are amended. In particular, claim 20 is amended to "consisting of" format and to incorporate the subject matter of dependent claims 21-22. Further support can be found in the disclosure, for example, at page 4, lines 16-28.

Claims 23 and 24 are amended to change their dependency.

Claim 25 is amended to incorporate claim 26. Further support can be found in the disclosure, for example, at page 4, lines 16-28.

Other minor editorial revisions have been made to the claims to better conform to U.S. claim form. Such revisions are non-substantive and not intended to narrow the scope of protection. Such revisions include: replacing the "characterized by" language with standard claim language, such as "wherein"; revising the beginning of the claims to recite "A" or "The" and

revising the claim language to provide proper antecedent basis throughout the claims.

No new matter has been added by the above claim amendments.

Claims 21-22 and 26-37 have been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any cancelled subject matter.

Claims 20, 23, 24, and 25 are pending upon entry of this amendment.

The specification is amended to include a new Sequence Listing in paper copy and computer readable form (CRF) for the sequences found in the disclosure. The specification has also been correspondingly amended to insert appropriate SEQ ID NOs where needed. The paper copy and CRF copy are the same and no new matter has been added. Support can be found in the sequences in the originally filed application. See the discussion below regarding the support for the newly added sequences therein.

The Abstract is amended to include the name of the enzyme as suggested by the Office. No new matter has been added.

Applicants are submitting the present Amendment without prejudice to the subsequent prosecution of claims to some or all of the subject matter which might be disclaimed by virtue of this response (although none is believed to be), and explicitly

reserve the right to pursue some or all of such subject matter, in Divisional or Continuation Applications.

Applicants thank the Examiner for the careful examination of this case and respectfully request reexamination and reconsideration of the case, as amended. Below Applicants address the rejections in the Office Action and explain why the rejections are not applicable to the pending claims as amended.

II. OBJECTION TO THE SPECIFICATION/SEQUENCE LISTING

The specification was objected to as failing to comply with the Sequence Rules for the reasons in item 5 on pages 4-5 of the Office Action. This objection is respectfully traversed.

In reply, please find herewith a new Sequence Listing (in paper copy and computer readable form (CRF)). Applicants have amended the specification to insert the new Sequence Listing and to insert SEQ ID NOs where appropriate. The paper copy and CRF copy are the same and no new matter has been added. The Sequence Listing was generated to include the sequences found in the originally filed application using PatentIn version 3.5 (September 2007). The Sequence Listing was run through Checker Version 4.4.0 (October 25, 2005) and no errors were found.

Kindly note the new Sequence Listing contains additional sequences corresponding to: the β-clamp of *E. coli* DNA polymerase III (SEQ ID NO 5); the RQLVLGL peptide in the last line on page 18 (SEQ ID NO 6); and the peptide biding site of the

binding site of the β-clamp of *E. coli* DNA polymerase III (SEQ ID NO 7). Applicants submit the new sequences in the Sequence Listing do not constitute new matter for the reasons noted below.

To start, in reply to the concerns in items 5(a)-(e) on pages 4-5 of the Office Action, Applicants note that, regarding the peptidic region of the β-clamp of *E. coli* DNA polymerase III (correspond to atoms 4045 to 5688 in the atomic coordinates disclosed in claim 24 and the other atomic coordinate in the specification), it is not possible to provide a SEQ ID NO thereof.

Indeed, as represented in the following Table 1, due to the spatial configuration, amino acids of the β-clamp of *E. coli* DNA polymerase III are not contiguous and never represent an amino acid sequence of at least 4 amino acids.

Table 1: amino acids interaction between beta residues and p16 residues

P16 residues	R10	Q11						V13		L12				
Interacting Beta residues	M364	H175	N320	Y323	M362	P363	M364	H175	M362	H175	V344	M362	P363	M364

P16 residues	L14								L16					
Interacting Beta residues	T172	R176	L177	V247	S346	V360	V361	M362	L155	T172	H175	L177	P242	V247

The above table 1 shows that 6 amino acids of the P16 peptide interact with one or more amino acids of the β-clamp, and

said amino acids of the β-clamp never constitute a contiguous amino acid chain of at least 4 amino acids.

However, the specification describes and provides working examples exemplifying of the β-clamp of *E. coli* DNA polymerase III and the binding region therein that interacts with the disclosed P16 peptide, even though it does not explicitly recite the amino acid sequences for such.

Further, it is respectfully submitted that the amino acid sequence of the β-clamp of *E. coli* DNA polymerase III was well known and a fully characterized prior to the filing date of the application. In other words, the protein was fully sequenced and the sequence was publicly known prior to the Applicants' filing date. As proof thereof, enclosed herewith is a copy of the NCBI page corresponding to DnaN protein (NP_418156) which was available since October 15, 2001. Also, enclosed is a copy of an online protein comparison between NP_418156 and SEQ ID NO 5, but using Blast2 online software available on the NCBI web site (http://blast.ncbi.nlm.nih.gov/bl2seq/wblast2.cgi), demonstrating that the two sequences share 100% identity.

As such, the skilled artisan could readily envision and obtain the known amino acid sequence for the β-clamp of *E. coli* DNA polymerase III based on the knowledge in the art and the support in the disclosure. Thus, there is support in the disclosure for new SEQ ID NO: 5, which corresponds to the β-clamp of *E. coli* DNA polymerase III.

Further, the specification describes the binding site of the β-clamp of *E. coli* DNA polymerase III, i.e., the amino acids interacting with the P16 peptide as included in the region delimited by the amino acids at the positions 155 to 364 (now SEQ ID NO: 7). The above mentioned region, i.e. 155-364, is represented by SEQ ID NO 7. See, for instance, the discussion of such in the disclosure, in Table 2 on page 20.

As such, the skilled artisan could readily envision and obtain the binding site of the β-clamp of *E. coli* DNA polymerase III (i.e., the amino acids at the positions 155 to 364 (now SEQ ID NO: 7) interacting with the P16 peptide. Thus, there is support in the disclosure for new SEQ ID NO: 7, which corresponds to the binding site of the β-clamp of *E. coli* DNA polymerase III.

For these reasons, Applicants believe the new sequences (SEQ ID NOS: 5 and 7) in attached revised Sequence Listing do not constitute new matter, as the newly added sequences therein are a based on the amino acid sequence of the β-clamp of *E. coli* DNA polymerase III, which was well known and a fully characterized prior to the filing date of the application.

Thus, it is respectfully submitted that the application complies with the Sequence Rules under 37 C.F.R. §§ 1.821-1.825. Therefore, the above-noted objection should be withdrawn.

III. OBJECTION TO THE SPECIFICATION/ABSTRACT

The Abstract was objected to on the basis that it does not completely describe the disclosed subject matter for the reasons in item 6 on page 6 of the Office Action. This objection is respectfully traversed.

The Abstract has been revised to include the full name of the enzyme as suggested by the Examiner. Therefore, the above-noted objection should be withdrawn.

IV. CLAIM OBJECTIONS

Claims 24 and 25 were objected for the reasons in items 7(a)-(b) on page 6 of the Office Action. This objection is respectfully traversed.

In reply to item 7(a), please see the above discussion (and Tables) as to why it is not possible to provide a SEQ ID NO for the atomic coordinates in claim 24. Again, as shown in Table 1, due to the spatial configuration, amino acids of the β-clamp of *E. coli* DNA polymerase III are not contiguous and never represent an amino acid sequence of at least 4 amino acids.

In reply to item 7(b), claim 25 has been amended to include the full name for MES, 2-(N-morpholino)ethane sulfonic acid, as suggested by the Office.

Therefore, the above-noted objections should be withdrawn.

V. INDEFINITENESS REJECTION

Claims 20-26 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons in item 8 on page 7 of the Office Action.

This rejection is respectfully traversed.

Claim 20 has been amended to remove the following rejected language "about 3 to about 30 amino acids" and "about 16 amino acids". Note amended claim 20 now recites a co-crystal with "a peptide of 16 amino acids." Due to the removal of this language, the amended claim should be clear as to the length of peptide. The claims are thus clear, definite and have full antecedent basis. Thus, the rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

VI. WRITTEN DESCRIPTION AND ENABLEMENT REJECTIONS

Claims 20-24 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for the reasons in item 9 on pages 7-10 of the Office Action.

Claims 25-26 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for the reasons in item 10 on pages 10-13 of the Office Action.

Claims 20-26 were similarly rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement for the reasons in item 11 on pages 13-19 of the Office Action.

It is noted that the grounds for the above rejections are essentially the same.

As to the first written description rejection and the enablement rejection, the Office argues that the specification does not provide written support, nor enabling support, for the broad genus of co-crystals containing the broad genus of peptides of varying length encompassed by the language "about 3 to about 30 amino acids" and "about 16 amino acids" without specifying the all criteria of all claimed crystals, such as space group, cell dimension and polypeptide definition. See the bottom of page 7 and pages 13-14 of the Action.

In the second written description rejection, the Office rejects the method of claims 25-26 on the basis the specification lacks written support for the claimed method for essentially the same reasons noted above regarding the breadth of the co-crystals produced by the claimed process.

Applicants traverse the rejections as applied to the amended claims.

For the sole purpose of expediting prosecution and not to acquiesce to these rejections, the claims have been

amended to correspond to the subject matter the Office noted is supported and enabled by the disclosure.

For instance, claim 20 has been amended to: (1) "consisting of" format; (2) remove the language "about 3 to about 30 amino acids" and "about 16 amino acids"; and (3) specify all characteristics of the claimed co-crystal. Accordingly, amended claim 20 now recites:

> **20**. A protein crystal consisting of:
>
> a processivity clamp factor of DNA polymerase that is the β subunit of DNA polymerase polymerase III of *Escherichia coli* and has the amino acid sequence of SEQ ID NO 5; and
>
> a peptide of 16 amino acids having the amino acid sequence of VTLLDPQMERQLVLGL (SEQ ID NO: 1),
>
> wherein said protein crystal is triclinic and has cell dimensions of: a = 41.23 Å, b = 65.22 Å, c = 73.38 Å, α = 73.11°, β = 85.58°, and γ = 85.80°.

In this sense, amended claim 20 now corresponds to what the Office noted is supported by the disclosure in the paragraph bridging pages 8-9 of the Action. This also corresponds to the subject matter noted as enabled at the bottom of page 13 of the Action.

It should be noted that the method claim 25 has been similarly amended: (1) to remove the language "about 3 to about 30 amino acids" and "about 16 amino acids"; (2) to specify all characteristics and elements of the ingredients and the resulting co-crystal; and (3) to recite a specific process.

As such, amended claim 25 now corresponds to the methods that the Office noted are supported in the disclosure, *i.e.*, the methods exemplified therein. See for instance, the top of page 12 of the Action and the discussion of Example 1-1 of the disclosure.

Therefore, the present amendment renders moot the above written description rejections and enablement rejection. Thus, the rejections should be withdrawn.

VII. ANTICIPATION REJECTIONS

Claim 20 was rejected under 35 U.S.C. § 102(b) as anticipated by JERUZALMI (Cell, vol. 106, pp. 417-428 (2001)) for the reasons in item 12 on pages 19-20 of the Office Action.

Claims 33-34 were rejected under 35 U.S.C. § 102(b) as anticipated by DALRYMPLE (WO200238596, published May 16, 2002) for the reasons in item 13 on pages 20-21 of the Office Action.

These rejections are respectfully traversed as applied to the amended claims.

As to the first anticipation rejection over claim 20, the Office argues the claim language "comprising", "about 3 to about 30 amino acids" and "about 16 amino acids" render the claims overly broad. The Office thus concludes the 140

amino acid peptide of JERUZALMI reads on "about 16 amino acids."

For the sole purpose of expediting prosecution and not to acquiesce to the rejection, claim 20 has been amended: (1) to "consisting of" format; and (2) to remove the language "about 3 to about 30 amino acids" and "about 16 amino acids". Accordingly, the present amendment obviates the Office's position and the rejection should thus be withdrawn.

As to the second anticipation rejection over claims 33-34, Applicants cancelled the rejected claims without prejudice or disclaimer thereto, and for the sole purpose of expediting prosecution and not to acquiesce to the rejection. Thus, the rejection is moot and should be withdrawn.

VIII. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

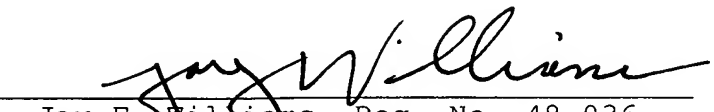
If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any

additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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JW/fb

APPENDIX:

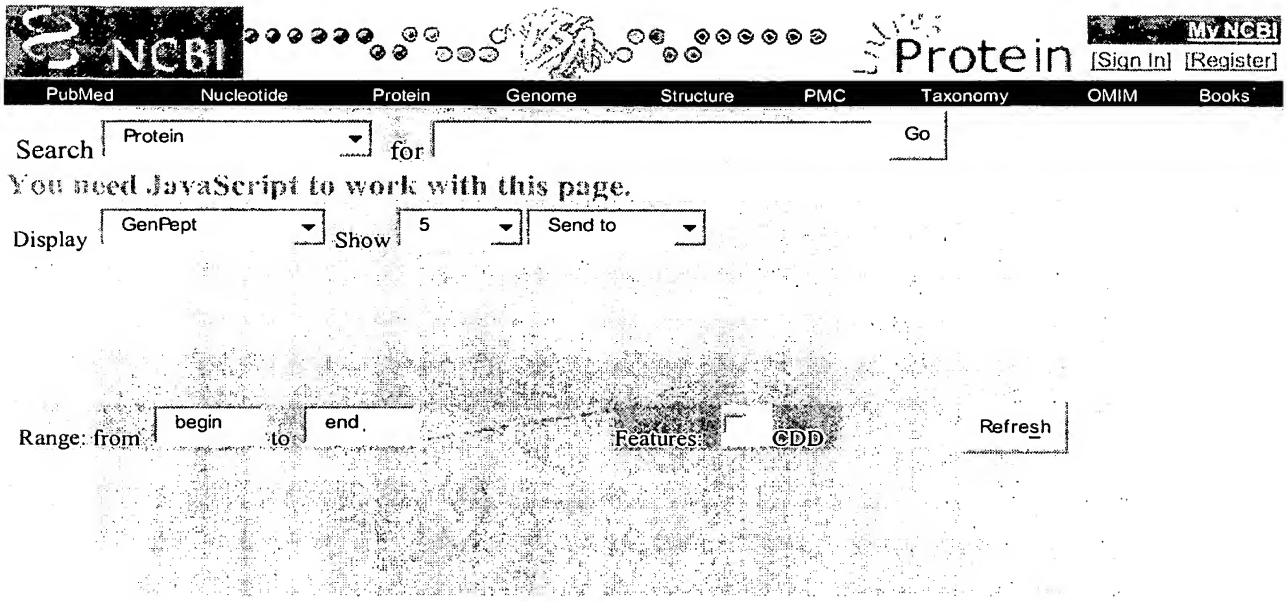
The Appendix includes the following item(s):

☒ - a new or amended Abstract of the Disclosure

☒ - a newly revised Sequence Listing in paper and computer readable form (CRF)

☒ - a copy of NCBI page corresponding to DnaN protein (NP_418156)

☒ - a copy of an online comparison between NP_418156 and SEQ ID NO:5.



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BLink, Conserved Domains, Links

- Comment
- Features
- Sequence

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            Bacteria; Proteobacteria; gamma subdivision; Enterobacteriaceae;
            Escherichia.
REFERENCE   1  (residues 1 to 366)
  AUTHORS   Blattner,F.R., Plunkett,G. III, Bloch,C.A., Perna,N.T., Burland,V.,
            Riley,M., Collado-Vides,J., Glasner,J.D., Rode,C.K., Mayhew,G.F.,
            Gregor,J., Davis,N.W., Kirkpatrick,H.A., Goeden,M.A., Rose,D.J.,
            Mau,B. and Shao,Y.
  TITLE     The complete genome sequence of Escherichia coli K-12
  JOURNAL   Science 277 (5331), 1453-1474 (1997)
  MEDLINE   97426617
REFERENCE   2  (residues 1 to 366)
  AUTHORS   NCBI Microbial Genomes Annotation Project.
  TITLE     Direct Submission
  JOURNAL   Submitted (26-SEP-2001) National Center for Biotechnology
            Information, NIH, Bethesda, MD 20894, USA
REFERENCE   3  (residues 1 to 366)
  AUTHORS   Blattner,F.R.
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TITLE Direct Submission
JOURNAL Submitted (02-SEP-1997) Guy Plunkett III, Laboratory of Genetics, University of Wisconsin, 445 Henry Mall, Madison, WI 53706, USA. Email: ecoli@genetics.wisc.edu Phone: 608-262-2534 Fax: 608-263-7459

REFERENCE 4 (residues 1 to 366)
AUTHORS Blattner,F.R.
TITLE Direct Submission
JOURNAL Submitted (16-JAN-1997) Guy Plunkett III, Laboratory of Genetics, University of Wisconsin, 445 Henry Mall, Madison, WI 53706, USA. Email: ecoli@genetics.wisc.edu Phone: 608-262-2534 Fax: 608-263-7459

COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final NCBI review. The reference sequence was derived from AAC76724. This sequence was determined by the E. coli Genome Project at the University of Wisconsin-Madison (Frederick R. Blattner, director). Supported by NIH grants HG00301 and HG01428 (from the Human Genome Project and NCHGR). The entire sequence was independently determined from E. coli K-12 strain MG1655. Predicted open reading frames were determined using GeneMark software, kindly supplied by Mark Borodovsky, Georgia Institute of Technology, Atlanta, GA, 30332 [e-mail: mark@amber.gatech.edu]. Open reading frames that have been correlated with genetic loci are being annotated with CG Site Nos., unique ID nos. for the genes in the E. coli Genetic Stock Center (CGSC) database at Yale University, kindly supplied by Mary Berlyn. A public version of the database is accessible (http://cgsc.biology.yale.edu/). Annotation of the genome is an ongoing task whose goal is to make the genome sequence more useful by correlating it with other data. Comments to the authors are appreciated. Updated information will be available at the E. coli Genome Project's World Wide Web site (http://www.genetics.wisc.edu/). *** The E. coli K-12 sequence and its annotations are periodically updated; this is version M54. No sequence changes. Annotation updates: updated gene identifications and products; all new functional assignments courtesy of Monica Riley; added promoters, protein binding sites, and repeated sequences described in reference 1. The unique numeric identifiers beginning with a lowercase 'b' assigned to each gene (protein- or RNA-encoding) are now designated as gene synonyms instead of labels. This should allow them to be searched for in Entrez as gene names.
Method: conceptual translation.

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Blast 2 Sequences results

PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.18 [Mar-02-2008]

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Masking character option X for protein, n for nucleotide Masking color option
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Show CDS translation Align

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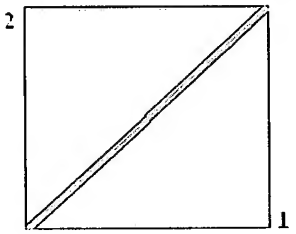

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Identities = 366/366 (100%), Positives = 366/366 (100%), Gaps = 0/366 (0%)

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